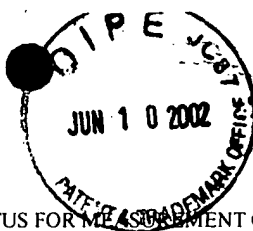


AMENDMENT AND RESPONSE

Serial Number: 09/367,859

Filing Date: September 2, 1999

Title: METHOD AND APPARATUS FOR MEASUREMENT OF BLOOD SUBSTITUTES



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CLEAN VERSION OF PENDING CLAIMS

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1. (Twice amended) A method of determining the concentration of a selected interferent contained in a specimen in the presence of a blood substitute, one or more other interferents, and at least one analyte, by quantification of the selected interferent in said specimen, using a spectrophotometer, comprising the steps of:

- B1
- i) generating a calibration algorithm for said selected interferent;
 - ii) measuring with said spectrophotometer, an absorbance of radiation by said selected interferent in said specimen; and
 - iii) incorporating said absorbance measured in step ii) in said algorithm and calculating the concentration of said selected interferent in said specimen.

5. (Amended) The method of claim 21 wherein said concentration of liberated Hb is determined in the presence of one or more additional interferents chosen from the group consisting of intralipid (IL), bilirubin (BR) and biliverdin (BV).

6. The method of claim 5 wherein said calibration algorithm for liberated Hb is:

$$\text{g/L Hb} = A(558) - B(570) + C(730) - D$$

where numbers in the parenthesis are the first derivative of absorbance at the wavelengths (nm) shown and A, B, C and D are constants.

B2

7. The method of claim 1, wherein said quantification includes calculation the first derivatives of at least two portions of a spectrum generated from a scan for a particular interferent which are used to calculate said selected interferent concentration.

8. (Previously Once Amended) A method of correcting for the concentration of a blood substitute interferent contained in a specimen having at least one analyte, using a spectrophotometer, comprising the steps of:

g/L Hb

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- i) generating a calibration algorithm for said blood substitute interferent;
- ii) generating an algorithm for said analyte which provides a relationship between a measured analyte concentration of said at least one analyte and an amount of said blood substitute interferent present in said specimen;
- iii) measuring with said spectrophotometer, an absorbance of radiation for said specimen with any blood substitute present in the specimen;
- iv) using said calibration algorithm and said absorbance measured in step (iii) to predict concentration of said blood substitute interferent present; and
- v) correlating the relationship from step ii) and the prediction from step (iv) to predict concentration of said at least one analyte as if no blood substitute interferent were present.

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9. The method of claim 8 wherein said specimen also contains one or more non-blood substitute interferents and wherein the concentration of said non-blood substitute interferent is also determined by:

- (i) generating a calibration algorithm for each of at least one non-blood substitute interferent;
- (ii) measuring the absorbance of radiation by said specimen; and
- (iii) correlating the absorbance measured in step (ii) to the amount of said non-blood substitute interferent.

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10. The method of claim 8 where the least one analyte is chosen from the group consisting of Na, K, Cl, HCO₃, Ca, Mg, creatinine, urea, total protein, gamma glutamyl transfurase (GGT), aspartate amino transfurase (AST), lactate dehydrogenase (LDH), creatine kinase (CK), alkaline phosphatase (ALP) and total bilirubin (Tbili).

11. The method of claim 8 where reflectance is used instead of absorbance.

12. The method of claim 8 where the radiation is in the range of 474-910 nm.

13. The method of claim 8 where calibration is conducted with samples containing all interferents expected during an analysis of an unknown sample.
14. The method of claim 12 where the sample contains an even distribution of interferents of interest, and the concentrations of any two interferents do not correlate significantly.
15. The method of claim 9 where said non-blood substitute interferent is selected from the group consisting of haemoglobin (Hb), bilirubin (BR), biliverdin (BV) and turbidity.
16. The method of claim 8 where the measured concentration of an analyte is correlated to an amount of blood substitute present by developing an appropriate linear regression equation in an analyzer.
- 32 17. A method of distinguishing true hemolysis from pseudo hemolysis caused by a blood substitute interferent comprising the steps of:
- identifying the presence of a blood substitute interferent contained in a specimen in the presence of Hb liberated from blood cells, turbidity and bile pigments, by quantification of the blood substitute in said specimen, using a spectrophotometer, comprising the steps of:
 - measuring absorbance of radiation by said interferent in said specimen; and
 - incorporating said absorbance measured in step a(i) in the following algorithm:
$$\text{g/L CL1 Hb} = A(541\text{nm}) - B(558\text{nm}) + C(600\text{nm}) - D(616\text{nm}) + E$$
where (Xnm) is the first derivative of absorbance measured at the wavelengths specified and A, B, C, D and E represent constants; and calculating the concentration of said interferent in said specimen; and
 - measuring Hb liberated from blood cells in the presence of said blood substitute interferent contained in a specimen, using a spectrophotometer, comprising the steps of:

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- (i) measuring absorbance of radiation by said specimen with said blood substitute interferent present; and
- (ii) incorporating said absorbance measured in step b(i) in the following algorithm:

$$g/L \text{ Hb} = A(558) - B(570) + C(730) - D$$

where numbers in the parenthesis are the first derivative of absorbance at the wavelengths (nm) shown, where A, B, C, and D are constants, and calculating the concentration said liberated Hb in said specimen.

32 18. The method of claim 17 wherein said concentration of liberated Hb is determined in the presence of one or more additional interferents chosen from the group consisting of intralipid (IL), bilirubin (BR) and biliverdin (BV).

19. (New) A method of determining an amount of a blood substitute in a specimen using a spectrophotometer, said specimen further comprising one, or more than one, analyte, and one, or more than one, interferent selected from the group consisting of haemoglobin liberated from blood cells, turbidity, and bile pigments, said method comprising:

- i) generating a calibration algorithm for said blood substitute;
- ii) measuring with said spectrophotometer, an absorbance of radiation by said blood substitute in said specimen; and
- iii) incorporating said absorbance measured in step ii) in said algorithm and calculating a concentration of said selected blood substitute in said specimen.

20. (New) The method of claim 19, where said blood substitute is cross linked haemoglobin (CLHb).

21. (New) A method of determining an amount of haemoglobin (Hb) in a specimen using a spectrophotometer, said haemoglobin liberated from blood cells, said specimen further comprising

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one, or more than one, analyte, and a blood substitute, said method comprising:

- i) generating a calibration algorithm for said Hb;
- ii) measuring with said spectrophotometer, an absorbance of radiation by said Hb in said specimen; and
- iii) incorporating said absorbance measured in step ii) in said algorithm and calculating the concentration of said Hb in said specimen.

22. (New) A method of determining a concentration of an analyte contained in a specimen in the presence of one, or more than one, interferent, using a spectrophotometer, comprising:

- i) generating a calibration algorithm for said one or more than one interferent;
- ii) measuring with said spectrophotometer, an absorbance of radiation by said one or more than one interferent in said specimen;
- iii) incorporating said absorbance measured in step ii) in said algorithm and calculating the concentration of said one or more than one interferent in said specimen to obtain an interferent concentration;
- iv) determining a concentration of said analyte in said specimen to obtain a preliminary analyte concentration; and
- v) correcting said preliminary analyte concentration for said interferent concentration to obtain said true concentration of said analyte.